REMARKS

Claims 34 and 36-69 are pending in this application. Claims 1-33 and 35 were previously cancelled without prejudice to or disclaimer of the subject matter contained therein. Claims 34, 36 and 37 were previously withdrawn as being directed to non-elected subject matter.

In view of the following, further and favorable consideration is respectfully requested.

I. Rejections under 35 U.S.C. §103(a)

A. Claims 38-46, 49-51 and 54 as being unpatentable over Hubbard et al. (U.S. Patent No. 7,060,287) in view of Janas et al. (U.S. Patent No. 6,451,059)

B. Claims 38, 47 and 48 as being unpatentable over Hubbard et al., in view of Janas et al. and Draenert (U.S. Patent No. 4,373,217)

C. Claims 38 and 51-53 as being unpatentable over Hubbard et al., in view of Janas et al. and Gertzman et al. (U.S. Patent No. 7,019,192)

D. Claims 55-66 and 69 as being unpatentable over Hubbard et al., in view of Draenert

E. Claims 55 and 66-68 as being unpatentable over Hubbard et al., in view of Gertzman et al.

The Examiner has presented the above identified obviousness rejections against the pending claims.

Applicants traverse each of these rejections. The requirements necessary to establish a *prima facie* case of obviousness were set forth in a previous response, i.e. the response filed on January 19, 2010, on pages 16-17, and are not repeated

herein for the sake of brevity.

Applicants maintain that a *prima facie* case of obviousness has not been established by the Examiner, because none of the cited references when taken alone or in any combination teach all of the limitations of the pending claims as required by *In re Wilson*.

Instant Claims

To summarize, all of the pending claims necessarily require a "resorbable implant" comprising microparticles of βTCP which are biodegradable in fibrous tissue within 2 to 36 months. For ease of reference, the two pending independent claims are reproduced below:

> **38**. (Previously Presented) A resorbable implant for subcutaneous or intradermal injection into fibrous tissue, comprising microparticles of one biocompatible ceramic compound in suspension in at least one vector fluid,
>
> wherein said microparticles are biodegradable, once the implantation has been made into the fibrous tissue, within a period of from 2 to 36 months and have a size of from 10 to 80 μm, said ceramic compound is tricalcium phosphate (βTCP) and has a specific surface area of from 0.5 m^2/g to 100 m^2/g, and said vector fluid comprises at least one compound based on hyaluronic acid and at least one biodegradable thixotropic compound with pseudoplastic properties.

> **55**. (Previously Presented) A resorbable implant for subcutaneous or intradermal injection into fibrous tissue, comprising microparticles of one biocompatible ceramic compound in suspension in at least one vector fluid,
>
> wherein said microparticles are biodegradable, once the implantation has been made into the fibrous tissue, within a period of from 2 to 36 months, have a size of from 10 to 80 μm, and are present in the vector fluid in a weight/volume proportion strictly greater than 0% and less than 15%,

said ceramic compound is tricalcium phosphate (βTCP), and
said vector fluid comprises at least one compound based on hyaluronic acid and at least one biodegradable thixotropic compound with pseudoplastic properties.

Each of the remaining claims, i.e. claims 39-54 and claims 56-69, depend either directly or indirectly from claim 38 or claim 55, thereby incorporating all the limitations of the respective base claim, as well as any intervening claim.

Hubbard et al.

Hubbard et al. teach a permanent, biocompatible material for soft tissue augmentation comprising a matrix of smooth, round, substantially spherical particles of a biocompatible ceramic material, where the ceramic material can be homogeneously suspended in a biocompatible, resorbable lubricious gel carrier comprising a polysaccharide. Hubbard et al. generally describes βTCP as a potential ceramic material which may be contained in the implant compositions disclosed therein, and each of hyaluronic acid and xanthan gum as a potential polysaccharide that can be added to the composition.

The implants of Hubbard et al. are of a ***permanent*** nature and preferably employ hydroxyapatite (HAP). Hubbard et al. teach HAP as being highly compatible to tissue and ***substantially nonresorbable***, thereby rendering the ceramic augmentation material permanent and repetitious augmentations unnecessary. *See*, Hubbard et al., col. 4, line 22 and col. 5, lines 47-52.

Likewise, the teachings of Hubbard et al. regarding hyaluronic acid and

xanthan gum for use as potential polysaccharides are incomplete in comparison to the instantly claimed subject matter. Specifically, Hubbard et al. do not teach the use of a combination of these two materials, i.e. hyaluronic acid-based compounds and thixotropic compounds. Hubbard et al. provide no compositions containing hyaluronic acid or a combination of any two or more polysaccharides.

Further, Hubbard et al. fails to teach the specific surface area of the ceramic compound, as well as the amounts of the microparticles according to the present claims.

Thus, with respect to the teachings of Hubbard et al., Applicants note the following:

- there is a clear teaching away from biodegradability/degradation due to the ***permanent*** nature of the implants taught therein;
- no biodegradability or time period for degradation is described for ßTCP (which is consistent with the permanence of the implants taught);
- no combinations of hyaluronic acid with a biodegradable thixotropic compound with pseudoplastic properties (such as a polysaccharide) are taught; and
- no specific surface area or overall amount of the ceramic compound is taught.

Secondary References

Janas et al. (US Patent No. 6,451,059)

Jana et al. teach a hard tissue scaffold comprising resorbable ceramic fibers. Janas et al. is cited by the Examiner to cure one of the deficiencies of Hubbard et al., namely the lack of any the teaching with respect to particle surface area. In this regard, Janas et al. teach particles of ceramic tricalcium phosphate ($Ca_3(PO_4)_2$), with a BET surface area of 1.708 m^2/g. *See*, Example 1.

However, this teaching is taken out of context of the broader teachings of Janas et al. Specifically, according to Janas et al., the tricalcium phosphate particles have an ***initial surface area*** of 1.708 m^2/g. However, these particles are then used to ***prepare ceramic fibers and scaffolds*** suitable for use in bone replacement, which is the entire object of the teachings of Janas et al. Accordingly, neither Hubbard et al. nor Janas et al. teach a resorbable implant comprising a ceramic compound that "has a specific surface area of from 0.5 m^2/g to 100 m^2/g."

Applicants respectfully submit that the introduction of the teachings of Janas et al. to supplement the shortcomings of Hubbard et al. still does not establish a *prima facie* case of obviousness against claims 38-46, 49-51 and 54. In the first instance, the Examiner's proposed reason for introducing Janas et al., i.e. the teaching of surface area, is not commensurate with the scope of the instant claims. Specifically, the particles of Janas et al. are in no way used as presently claimed and are not present in the product of Janas et al. in the same form as recited in the instant claims.

Furthermore, both Hubbard et al. and Janas et al. are directed to ***permanent*** tissue modification. Thus, the instantly claimed microparticles capable of

biodegrading within a period of 2 to 36 months from implantation are clearly not shown by this combination of references. In part, it is the large surface area of the instant microporous ceramic particles (i.e., 0.5 m^2/g to 100 m^2/g) that affords the ability of the presently claimed implant to be bioresorbable. In contrast, the particles of Hubbard et al. are smooth and non-porous, as well as round and substantially spherical. Applicants submit that while the instant technologies taught in these cited references are *generally* related to the claimed subject matter, there is nothing in either which would lead one of ordinary skill in the art to modify the teachings of two references relating *entirely* to permanent tissue repair to arrive at the instantly claimed subject matter relating to bioresorbable implants.

Thus, the combination of Hubbard et al. and Janas et al. fail to teach an implant comprising ***microparticles*** of tricalcium phosphate having a specific ***surface area*** of ***0.5 to 100 m^2/g*** which are capable of ***biodegrading*** in the tissue within a period of ***2 to 36 months*** after implantation, as required by claim 38 and the claims dependent therefrom.

Furthermore, a person of ordinary skill in the art trying to make a bioresorbable implant would have no reason to look to or rely upon teachings related to permanent implants such as those described in Hubbard et al. and Janas et al. In fact, the Examiner has still not identified any reason why a person of ordinary skill would combine the elements of Hubbard et al. and Janas et al. in a manner according to the subject matter of the instant claims.

Accordingly, the combination of Hubbard et al. in view of Janas et al. does not establish a *prima facie* case of obviousness against claims 38-46, 49-51 and 54, at least because each and every element of claim 38 is not taught. Therefore, the rejected claims are nonobvious within the meaning of 35 U.S.C. §103(a).

Draenert (U.S. Patent No. 4,373,217)

Draenert teach an implantation material comprising a polymeric base of an acrylate, a polymethacrylate, a copolymer of an acrylate and a methacrylate or a mixture thereof, and 5-35% by weight of resorbable tricalcium phosphate. This reference is cited by the Examiner to cure the deficiency of Hubbard et al. relating to the lack of teaching with respect to the amount of ceramic material present.

The teachings of Hubbard et al. and Janas et al. are discussed above and those comments are incorporated herein by reference. Specifically, Applicants have noted the following deficiencies in Hubbard et al.:

- there is a clear teaching away from biodegradability/degradation due to the ***permanent*** nature of the implants taught therein;
- no biodegradability or time period for degradation is described for ßTCP (which is consistent with the permanence of the implants taught);
- no combinations of hyaluronic acid with a biodegradable thixotropic compound with pseudoplastic properties (such as a polysaccharide) are taught; and

- no specific surface area or overall amount of the ceramic compound is taught.

Janas et al., introduced by the Examiner to show a specific surface area, did not remedy the deficiencies of Hubbard et al. as shown above.

Applicants respectfully submit that even assuming *arguendo* the teachings of Draenert show the instantly claimed amount of the microparticles, Draenert does not cure the remaining deficiencies of Hubbard et al. Specifically, Draenert teaches ***stable implantation materials***, i.e. bone cements. See, col. 1, lines 1 to 13 and col. 2, lines 23-30. The stable implantation materials taught by Draenert are used in bone replacement and bonding, as well as prosthesis anchoring materials, which are ***permanent*** structures.

Again, the instantly claimed microparticles capable of biodegrading within a period of 2 to 36 months from implantation are clearly not shown by this combination of references. In part, it is the large surface area of the instant microporous ceramic particles (i.e., 0.5 m^2/g to 100 m^2/g) that affords the ability of the presently claimed implant to be bioresorbable. In contrast, the particles of Hubbard et al. are smooth and non-porous, as well as round and substantially spherical. While the instant technologies taught in these cited references are *generally* related to the claimed subject matter, there is nothing in any of the cited references which would lead one of ordinary skill in the art to modify the teachings of these three references relating *entirely* to permanent tissue and bone repair to arrive at the instantly claimed subject

matter relating to bioresorbable implants.

Thus, the combination of Hubbard et al., Janas et al. and Draenert fail to teach an implant comprising ***microparticles*** of tricalcium phosphate having a specific ***surface area*** of ***0.5 to 100 m^2/g*** which are capable of ***biodegrading*** in the tissue within a period of ***2 to 36 months*** after implantation, as required by claims 38, 47 and 48.

Accordingly, the combination of Hubbard et al. in view of Janas et al. and Draenert does not establish a *prima facie* case of obviousness against claims 38, 47 and 48, at least because each and every element of claim 38 is not taught. Therefore, the rejected claims are nonobvious within the meaning of 35 U.S.C. §103(a).

The Examiner has also used the combination of Hubbard et al. and Draenert to reject claims 55-66 and 69. However, as stated above, Draenert does not remedy the deficiencies of Hubbard et al. with respect to the biodegradable nature of the claimed subject matter.

Thus, the combination of Hubbard et al. and Draenert fails to teach an implant comprising ***microparticles*** of tricalcium phosphate which are capable of ***biodegrading*** in the tissue within a period of ***2 to 36 months*** after implantation, as required by claims 55-66 and 69. In fact, the disclosures of Hubbard et al. and Draenert actually reinforce each other in teaching away from the present claims, as

both references relate *specifically* to permanent or stable implants, whereas the present claims are directed solely to resorbable implants.

Accordingly, the combination of Hubbard et al. in view of Draenert does not establish a *prima facie* case of obviousness against claims 55-66 and 69, at least because each and every element of claim 55 is not taught. Therefore, the rejected claims are nonobvious within the meaning of 35 U.S.C. §103(a).

Gertzman et al. (U.S. Patent No. 7,019,192)

Gertzman et al. teach a formable bone composition for application to a bone defect site to promote new bone growth at the site which comprises a new bone growth inducing compound of demineralized lyophilized allograft bone particles. This reference has been cited by the Examiner as teaching sodium hyaluronate carriers for the formable bone composition having a molecular weight of $6.6X10^5$ - $2.6X10^6$.

The teachings of Hubbard et al. are discussed above and those comments are incorporated herein by reference. The deficiencies of Hubbard et al. as noted by Applicants are:

- there is a clear teaching away from biodegradability/degradation due to the ***permanent*** nature of the implants taught therein;
- no biodegradability or time period for degradation is described for ßTCP (which is consistent with the permanence of the implants taught);
- no combination of hyaluronic acid with a biodegradable thixotropic

compound with pseudoplastic properties (such as a polysaccharide) are taught; and

- no specific surface area or overall amount of the ceramic compound is taught.

Janas et al., which was introduced to show a specific surface area of the ceramic particles, did not remedy the deficiencies of Hubbard et al. as shown above.

Applicants respectfully submit that even assuming *arguendo* the teachings of Gertzman et al. show the instantly claimed molecular weight of hyaluronic acid, Gertzman et al. do not cure the remaining deficiencies of Hubbard et al. Specifically, Gertzman et al. teach ***formable bone compositions.*** The compositions taught by Gertzman et al. do not show an implant comprising βTCP which is biodegradable in within 2 to 36 months of implantation. Furthermore, Gertzman et al. fails to teach the use of the hyaluronic acid compound *in combination* with a thixotropic compound (such as a xanthan-based compound or a cellulose derivative), as instantly claimed.

The instant microparticles capable of biodegrading within a period of 2 to 36 months after implantation are clearly not shown by this combination of references. In part, it is the large surface area of the instant microporous ceramic particles (i.e., 0.5 m^2/g to 100 m^2/g) that affords the ability of the presently claimed implant to be bioresorbable. In contrast, the particles of Hubbard et al. are smooth and non-porous, as well as round and substantially spherical. While, as in the previous instances, the subject matter of the cited references *generally* relates to the claimed subject matter,

there is nothing in any of the cited references which would lead one of ordinary skill in the art to modify the teachings contained therein to arrive at the instantly claimed subject matter relating to bioresorbable implants.

Thus, the combination of Hubbard et al., Janas et al. and Gertzman et al. fail to teach an implant comprising ***microparticles*** of tricalcium phosphate having a ***specific surface area*** of ***0.5 to 100 m^2/g*** which are capable of ***biodegrading*** in the tissue within a period of ***2 to 36 months*** after implantation, as required by claims 38 and 51-53.

Accordingly, the combination of Hubbard et al. in view of Janas et al. and Gertzman et al. does not establish a *prima facie* case of obviousness against claims 38 and 51-53, at least because each and every element of claim 38 is not taught. Therefore, the rejected claims are nonobvious within the meaning of 35 U.S.C. §103(a).

The Examiner has also used the combination of Hubbard et al. and Gertzman et al. to reject claims 55 and 66-68. However, as stated above, Gertzman et al. do not remedy the deficiencies of Hubbard et al. with respect to the biodegradable nature of the claimed subject matter.

Thus, the combination of Hubbard et al. and Gertzman et al. fails to teach an implant comprising ***microparticles*** of tricalcium phosphate which are capable of ***biodegrading*** in the tissue within a period of ***2 to 36 months*** after implantation, as

required by claims 55 and 66-68.

Accordingly, the combination of Hubbard et al. in view of Draenert does not establish a *prima facie* case of obviousness against claims 55 and 66-68, at least because each and every element of claim 55 is not taught. Therefore, the rejected claims are nonobvious within the meaning of 35 U.S.C. §103(a).

CONCLUSION

In view of the foregoing, Applicants submit that the pending claims are in condition for allowance. Early notice to this effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed such contact will expedite the prosecution of the application.

If the Examiner has any questions or comments regarding this matter, he is welcomed to contact the undersigned attorney at the below-listed number and address.

In the event this paper is not timely filed, applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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